

Thyroid colloid and microsomes, gastric parietal cells, mitochondria, and antinuclear factor persistently negative. Immunoglobulins: IgM 20 mg/100 ml (normal 47–170); IgA and IgG normal. X-rays: tomograms 1969 and thoracic inlet 1972 – no thymic tumour shown.

The following tests were negative or normal: blood film and ESR; plasma proteins and electrophoresis; lymphocyte function tests (phyto-haemagglutinin, mixed lymphocyte reaction, candida antigen); Rose Waaler, latex RA; thyroid and adrenal function tests; muscle biopsy.

Comment

Many distinct conditions have arisen in this patient in the last sixteen years: 1957, ulcerative colitis; 1960, lichen planus; 1969, myasthenia gravis; 1971, alopecia areata; 1973, LE cells in moderate numbers, splenomegaly and vitiligo.

Autoantibodies have been demonstrated in ulcerative colitis (Broberger & Perlmann 1959) and myasthenia gravis (Beutner *et al.* 1962). These diseases are presumed by some to be manifestations of autoimmunity. Myasthenia gravis has been associated with other such diseases (Simpson 1964). Alopecia areata is likewise thought by some to be of the same nature, and has been associated with the organ-specific autoimmune diseases (Stankler & Bewsher 1972), ulcerative colitis and vitiligo (Muller & Winkelmann 1963, Lerner 1971).

The nature of the skin eruption is debatable. The diagnosis of lichen planus was made on the histopathology, as clinically it was atypical. If this is lichen planus, then its close temporal association with this group of conditions may be of etiological significance. Lichen planus has been remarkably free of reported associations with other conditions whether dermatological or internal. Copeman *et al.* (1970) described 4 cases in which it was impossible clinically or histopathologically to make a firm diagnosis between lichen planus or lupus erythematosus (LE). All 4 subsequently progressed to LE. In many respects this case is similar. The dense band-like lymphocytic infiltration with basal cell liquefaction on which the original diagnosis of lichen planus was made could have been due to LE. LE cells have, however, only appeared recently combined with splenomegaly. The association of LE with myasthenia gravis and ulcerative colitis is also recognized (Alarcón-Segovia *et al.* 1963, White & Marshall 1962).

The association of these separate disorders is not necessarily fortuitous and there may be some basic defect in the patient's immunological status, whereby multiple autoimmune conditions arise. This could result from an underlying thymic abnormality. The thymus, according to Burnet (1962), is important in preventing formation of

autoantibodies; it is well recognized that 60–70% of cases of myasthenia gravis are associated with thymic abnormalities (White & Marshall 1962). It may be that at a future date a thymoma will develop. Conversely, the remarkable improvement in the myasthenia since the severe exacerbation four years ago could have been the result of a 'medical thymectomy', precipitated by the many different stresses suffered at that time.

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Thymoma, Acquired Hypogammaglobulinæmia, Lichen Planus, Alopecia Areata

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F H, man aged 67

History: Transient ptosis in 1959 – no cause found. Thymoma discovered in 1965. Thymectomy performed. *Histology:* well-differentiated lymphoepitheliomatous tumour with a good fibrous capsule. Onset of bilateral basal bronchiectasis in 1967, confirmed by chest X-ray and bronchogram, which has progressed with frequent pneumonic complications. Oral lichen planus appeared a year later associated with nail destruction and lesions on the trunk. The oral lesions became erosive in 1969 and have persisted with large areas of tongue frequently involved (Fig 1). Low levels of gamma globulins were first noticed in 1971 and the levels have continued to fall. Alopecia areata developed in 1972. Recently, *Trichophyton mentagrophytes* has been isolated from his groins and feet. The patient has reacted to transfusions of whole blood and reconstituted pooled dried plasma, but is able to tolerate fresh frozen plasma. Weight loss 25 kg in the last three years.

Treatment: 1971–72: systemic steroids for oral erosive lichen planus, often in large doses. Since February 1973: regular plasma exchange transfusions every 3–4 weeks using a continuous flow

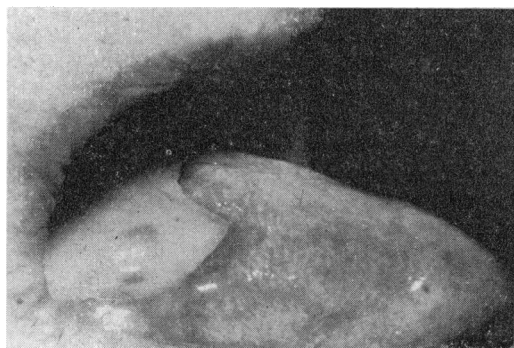


Fig 1 Extensive erosion on tongue

'Celltrifuge' blood cell separator. Prednisone 5 mg once daily, ampicillin 1 g four times daily. Adcortyl in Orabase, Whitfield's ointment.

Progress: Lichen planus of mouth and skin improved but new lesions still appear. Alopecia areata extended. Bronchiectasis marginally improved. Slow weight gain.

On examination: mouth – occasional small erosions; white streaks on lips and buccal mucosa; nails – destruction and clubbing; resolving lichen planus on trunk and hands; scalp and eyebrow – extensive alopecia areata.

Investigations: Serum immunoglobulin levels are shown in Table 1. Stimulated salivary IgA 4 mg/100 ml (normal 3–20); Iso-agglutinin titres (Blood Group O) Anti-A 1:2, -B 1:1 (both low); strong cytotoxic antibodies to leukocytes. Autoantibodies persistently negative to the following: thyroid colloid and microsomes, gastric parietal cells, smooth muscle, mitochondria, antinuclear factor. Complement normal. Lymphocyte function: normal response to PHA, mixed lymphocyte reaction, candida antigen, candida killing, nitro-blue tetrazolium.

Histopathology: 1973: Dorsum of hands and abdomen. Both sections show classical lichen planus. Numerous Civatte colloid-like bodies are

present not only at the epidermodermal junction but also throughout all layers of the epidermis and even in the stratum corneum (Fig 2A–C).

Other investigations: Haemoglobin 9.1–10.7 g/100 ml ESR 38–42 mm in 1 hour (Wintrobe), barium meal – distal stomach consistent with gastritis. The following tests were negative or normal: bone marrow, skeletal survey, LE cells, Rose Waaler, Coombs' test, Bence Jones protein, B₁₂ folate, Synacthen stimulation, Mantoux 1:1000.

Table 1

Concentration of serum immunoglobulin

	IgG (mg/100 ml)	IgA (mg/100 ml)	IgM (mg/100 ml)
Normal range	500–1600	125–425	47–170
July 1971	480	43	0
August 1972	420	26	49
October 1972	310	64	18
January 1973	250	35	18

Comment

The following features shown by this patient are well recognized: (1) Acquired hypogammaglobulinaemia and thymoma (Hobbs 1968), the former persisting even after thymectomy (Peterson *et al.* 1965); an underlying abnormality affecting both the immunoglobulin-producing lymphocytes and the thymus seems to be present. (2) The apparent paradox of a thymic abnormality associated with normal cellular but abnormal humoral lymphocytic responses (Asherson & Webster 1971). (3) The development of autoimmune diseases associated with hypogammaglobulinaemia and antibody deficiency states (Fudenberg 1971). (4) Autoimmune diseases appearing after thymectomy (Peterson *et al.* 1965).

There seems to be not only an underlying derangement in immunoglobulin production but also an abnormality in the mechanism of self-recognition (Fudenberg 1966). Although protective antibodies may be absent, accounting for

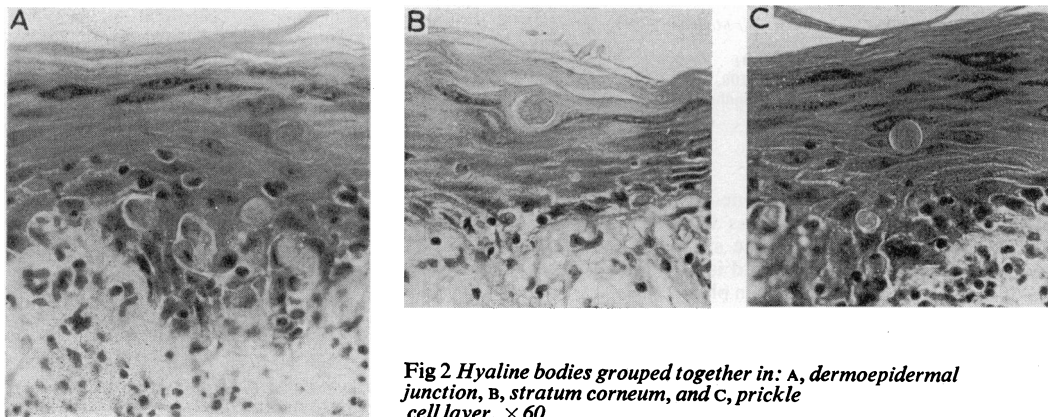


Fig 2 Hyaline bodies grouped together in: A, dermoepidermal junction, B, stratum corneum, and C, prickle cell layer. × 60

the progressive late onset bronchiectasis (Squire 1962), autoantibodies and allergic manifestations still occur (Wollheim *et al.* 1964). The patient has suffered from repeated transfusion reactions due to strong cytotoxic antibodies to leukocytes. It is therefore of interest that both lichen planus and alopecia areata have developed in this context, and have both been particularly aggressive.

The skin histopathology shows numerous colloid-hyaline-Civatte-like bodies in the dermo-epidermal region, and there is a definite tendency for grouping (Fig 2A). Similar discrete eosinophilic structures are present throughout all layers of the epidermis, even the stratum corneum (Fig 2B). Some of these may be related to sweat ducts and could be due to inspissated secretions. Those in the prickle cell layer are not, however, surrounded by a ductal arrangement of cells (Fig 2C). The bodies were predominantly PAS negative, and were quite separate from the stained sweat ducts. Direct immunofluorescent techniques on cryostat sections failed to show deposits of immunoglobulins or complement on these structures. These findings differ from those of Ueki (1969).

It seems that, whatever their nature, the bodies are being extruded unchanged on to the skin surface. These unusual features may be related to the fact that, in this patient, lichen planus has developed on a background of impaired immune reactivity. The grouping of these structures, their extrusion unchanged, and their presence in large numbers in a patient with immune deficiency may provide further evidence for their viral nature (Thyresson & Moberger 1957).

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Dr P D Samman: I have seen one other patient with myasthenia gravis who also has lichen planus. He started with lichen planus some six years ago then developed myasthenia gravis and is now losing most of his nails as a result of the lichen planus.

Dr C M Ridley: Dr Arnold Bloom has under his care at the Whittington Hospital a woman born in 1901 whose mother and maternal grandmother had diabetes. Vitiligo developed in 1929 and she went grey

in about 1941. Diabetes mellitus was diagnosed in 1965, idiopathic Addison's disease in 1966 and pernicious anaemia also in 1966. Antibodies to adrenal and parietal cells present (antinuclear factor negative, no antibodies to thyroid, smooth muscle or mitochondria). In 1965 she was seen by Dr P J Hare and was found to have widespread lichen planus. This involved the scalp with complete hair loss. The lichen planus cleared in a few months but the hair has not regrown. The scalp now shows some atrophy and scarring. She did not develop alopecia areata. This patient was reported by Turner & Bloom (1968 *Postgraduate Medical Journal* 44, 555-558).

Fixed Drug Eruption Due to 'Nonabsorbable' Sulphonamides

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LG, woman aged 62

History: Recurrent painful eruptions at the same sites on the dorsum of both hands for 2½ years. The eruption was initially bullous and recently erythematous and associated with oedema of the hands. Macular areas of hyperpigmentation persist between attacks (Fig 1). The mouth was occasionally affected. She has repeatedly and emphatically denied taking any drugs or medicines, and has been challenged on two separate occasions whilst still in hospital with eighteen different drugs including sulphadimidine, all of which failed to induce an attack. Due to the distressing symptoms she was given two separate courses of prednisone (for 8 months and 4 weeks) but with no benefit. Eventually, after 2½ years she admitted to taking Cremostrep (succinyl sulphathiazole 500 mg/5 ml, streptomycin 50 mg/5 ml) for her bowels, but was adamant that this product was not associated with the attacks. In the last few months she has developed a clothing dermatitis.

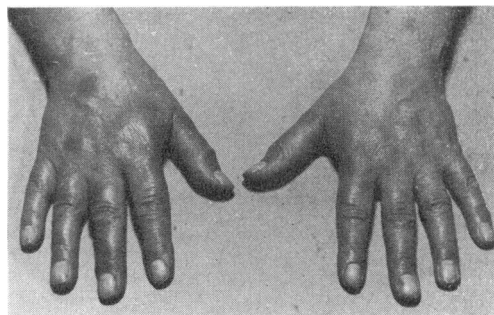


Fig 1 Persistent macular hyperpigmentation on dorsum of hands between attacks